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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/826,909	04/19/2004	Shailaja Kasibhatla	1735.0840002/RWE/ALS	1721

26111 7590 10/17/2007

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EXAMINER	
DUFFY, BRADLEY	

ART UNIT	PAPER NUMBER
1643	

MAIL DATE	DELIVERY MODE
10/17/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/826,909	KASIBHATLA ET AL.	
	Examiner	Art Unit	
	Brad Duffy	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 April 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-14,16-18 and 20-47* is/are pending in the application.

4a) Of the above claim(s) *1-13, 16-18 and 32-46* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *14,20-31 and 47* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☒ Other: *Exhibits A and B*.

DETAILED ACTION

1. The amendment filed April 26, 2007, is acknowledged and has been entered. Claims 15 and 19 have been cancelled. Claims 14, 20, 22, 26, 28, 30, and 31 have been amended. Claim 47 is newly added.

2. Claims 1-14, 16-18, 20-47 are pending in the application.

3. Claims 1-13, 16-18 and 32-46 have been withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on November 20, 2006.

4. Claims 14, 20-31 and 47 are under examination.

5. The following Office action contains NEW GROUNDS of rejection necessitated by amendment.

Priority

6. Applicant's claim under 35 USC §§ 119 and/or 120 for benefit back to the earlier filing date of U.S. Provisional Application No. 60/463,649, filed April 18, 2003, is acknowledged.

However, claims 14, 20-31 and 47 do not properly benefit under 35 U.S.C. §§ 119 and/or 120 by the earlier filing dates of the priority documents claimed, since those claims are rejected under 35 U.S.C. § 112, first paragraph, as lacking adequate written description and/or a sufficiently enabling disclosure.

To receive benefit of the earlier filing date under 35 USC §§ 119 and/or 120, the later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original

nonprovisional application or provisional application); the disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

In addition, it is noted that the claims do not properly benefit under 35 U.S.C. §§ 119 and/or 120 by the earlier filing dates of the priority documents claimed, since they do not disclose a Transferrin Receptor Related Apoptosis Inducing Protein (TRRAIP) "encoded by" the amino acid sequence of SEQ ID NO:1, 2, 3 or 8 (see the below new matter rejection of the claims under 35 U.S.C. 112, first paragraph).

Accordingly, the effective filing date of the claims is deemed the filing date of the instant application, namely April 19, 2004.

Grounds of Objection and Rejection Withdrawn

7. Unless specifically reiterated below, Applicant's amendment and/or arguments filed April 26, 2007, have obviated or rendered moot the grounds of objection and rejection set forth in the previous Office action mailed August 30, 2006.

Notably, claim 14 has been amended to recite "a Transferrin Receptor Related Apoptosis Inducing Protein (TRRAIP) *encoded*[1] by SEQ ID NO:1, 2, 3 or 8". Although it cannot be ascertained how a Transferrin Receptor Related Apoptosis Inducing Protein (TRRAIP) is *encoded* by an amino acid sequence[2], the previous prior art rejections have nonetheless been rendered moot by this amendment as the prior art cited does not teach or fairly suggest "a Transferrin Receptor Related Apoptosis Inducing Protein (TRRAIP) *encoded* by SEQ ID NO:1, 2, 3 or 8".

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[1] Italicized for emphasis
[2] see below rejection of the claims under 35 U.S.C. 112, second paragraph

Ground of Objection Maintained

Specification

8. The objection to the specification because the use of improperly demarcated trademarks is maintained. Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner that might adversely affect their validity as trademarks. See MPEP § 608.01(v).

Although it appears that Applicant has made a *bona fide* attempt to resolve this issue by appropriately amending the specification, additional examples of improperly demarcated trademarks appearing in the specification are noted, namely Sepharose® (see e.g., page 169, line 2) and Tween® (see e.g., page 164, line 3).

Again, appropriate correction is required. Each letter of a trademark should be capitalized or otherwise the trademark should be demarcated with the appropriate symbol indicating its proprietary nature (e.g., ™, ®), and accompanied by generic terminology. Applicants may identify trademarks using the "Trademark" search engine under "USPTO Search Collections" on the Internet at <http://www.uspto.gov/web/menu/search.html>.

Grounds of Rejection Maintained

Claim Rejections - 35 USC § 112

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. The rejection of claims 14, 20-31 and 47 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement, is maintained. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant

art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

This is a "written description" rejection.

At page 24 of the amendment filed April 26, 2007, Applicant has traversed the propriety of this ground of rejection.

Applicant's arguments have been carefully considered but are not found persuasive for the following reasons:

Again, the considerations that are made in determining whether a claimed invention is supported by an adequate written description are outlined by the published Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, para. 1, ``Written Description" Requirement (Federal Register; Vol. 66, No. 4, January 5, 2001; hereafter "Guidelines"). A copy of this publication can be viewed or acquired on the Internet at the following address: <http://www.gpoaccess.gov/>.

As amended, the claims are drawn to processes comprising contacting a structurally and functionally undefined Transferrin Receptor Related Apoptosis Inducing Protein (TRRAIP) encoded by SEQ ID NOS:1, 2, 3 or 8 and a detectably labeled gambogic acid (GA) or GA-related compound; and (b) monitoring whether said one or more test compounds displaces said GA or GA-related compound and binds to said TRRAIP wherein compounds which bind said TRRAIP are potentially therapeutic anticancer compounds.

At pages 24-25, Applicant has argued that amending claim 14 to recite "a Transferrin Receptor Related Apoptosis Inducing Protein (TRRAIP) *encoded* by SEQ ID NO:1, 2, 3 or 8" has rendered this ground of rejection moot.

In response, as set forth in the below rejection of the claims under 35 U.S.C. 112, second paragraph, it cannot be ascertained how the amino acid sequence of SEQ ID NO:1[3] encodes a Transferrin Receptor Related Apoptosis Inducing Protein as nucleotide sequences encode proteins. Therefore, it is

[3] In Applicants response to the restriction requirement filed 11/20/2006, Applicant submitted an alignment of SEQ ID NOs:1, 2, 3 or 8 showing that these amino acid sequences are identical.

submitted that the claims are drawn to a structurally and functionally diverse genus of Transferrin Receptor Related Apoptosis Inducing Proteins and as one of skill in the art could not immediately envision, recognize or ascertain how SEQ ID NO:1 encodes a Transferrin Receptor Related Apoptosis Inducing Protein, one of skill in the art could not immediately envision, recognize or ascertain the Transferrin Receptor Related Apoptosis Inducing Protein to which the claims are directed. Accordingly, one of skill in the art would not recognize that Applicant was in possession of the claimed invention.

Similarly, in response to Applicant's arguments on pages 25-27 that test compounds that bind and displace gambogic acid from a Transferrin Receptor Related Apoptosis Inducing Protein (TRRAIP) encoded by SEQ ID NO:1 are adequately described by this amendment, since one of skill in the art could not ascertain how SEQ ID NO:1 encodes a Transferrin Receptor Related Apoptosis Inducing Protein, one of skill in the art would not be able to immediately envision, recognize or ascertain which test compounds have these properties, let alone if compounds with these properties would be potentially therapeutic anticancer compounds.

Accordingly, after careful and complete consideration, contrary to Applicant's arguments, for these reasons and as explained more fully in the Office action mailed November 6, 2006, the specification as filed does not adequately describe a Transferrin Receptor Related Apoptosis Inducing Protein (TRRAIP) encoded by SEQ ID NO:1 to which the claims are directed and this rejection is maintained.

11. The rejection of claims 14, 20-31 and 47 under 35 U.S.C. 112, first paragraph, because the specification, **while being enabling for using** a method for identifying potentially therapeutic anticancer compounds, said method comprising contacting "transferrin receptor protein" (i.e., the polypeptide of any of SEQ ID NOs: 1, 2, 3 or 8) with gambogic acid (GA) or structurally-related test

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Therefore, it is merely redundant to refer to each sequence and any reference to SEQ ID NO:1

compounds that have or retain the ability to bind the protein and determining whether said contact induces a cancer cell expressing the protein to undergo apoptosis, whereby if the cancer cell undergoes apoptosis the compound is identified as a potentially therapeutic anticancer compound, **does not reasonably provide enablement for using** the claimed processes, is maintained. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

Starting at page 27 of the amendment filed April 26, 2007, Applicant has traversed this ground of rejection.

Applicant's arguments traversing the ground of rejection set forth in the preceding Office action have been carefully considered but not found persuasive to obviate this rejection.

M.P.E.P. § 2164.01 states:

> The standard for determining whether the specification meets the enablement requirement was cast in the Supreme Court decision of *Mineral Separation v. Hyde*, 242 U.S. 261, 270 (1916) which postured the question: is the experimentation needed to practice the invention undue or unreasonable? That standard is still the one to be applied. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). Accordingly, even though the statute does not use the term "undue experimentation," it has been interpreted to require that the claimed invention be enabled so that any person skilled in the art can make and use the invention without undue experimentation. *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988).

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue". These factors, which have been outlined in the Federal Circuit decision of *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988), include, but are not limited to, the nature of the invention, the state of the prior art, the relative skill of those in the art, the amount of direction or guidance disclosed in the specification, the presence or absence of working examples, the predictability or unpredictability of the art, the breadth of the claims, and the

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applies to SEQ ID NOs: 2, 3 and 8 as well.

quantity of experimentation which would be required in order to practice the invention as claimed. See also *Ex parte Forman*, 230 USPQ 546 (BPAI 1986). The amount of guidance, direction, and exemplification disclosed in the specification, as filed, would not be sufficient to enable the skilled artisan to use the claimed invention at the time the application was filed without undue and/or unreasonable experimentation.

As set forth above, as amended the claims are drawn to processes comprising contacting a Transferrin Receptor Related Apoptosis Inducing Protein (TRRAIP) encoded by SEQ ID NOS:1, 2, 3 or 8 and a detectably labeled gambogic acid (GA) or GA-related compound; and (b) monitoring whether said one or more test compounds displaces said GA or GA-related compound and binds to said TRRAIP wherein compounds which bind said TRRAIP are potentially therapeutic anticancer compounds.

At page 28 Applicant has argued that the amendment of claim 14 to recite contacting a Transferrin Receptor Related Apoptosis Inducing Protein (TRRAIP) encoded by SEQ ID NOS:1, 2, 3 or 8 and a detectably labeled gambogic acid (GA) or GA-related compound with one or more test compounds has enabled the claimed invention.

In response as discussed above in the rejection of the claims under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement one of skill in the art could not ascertain how SEQ ID NO:1 encodes a Transferrin Receptor Related Apoptosis Inducing Protein (TRRAIP), as SEQ ID NO:1 is an amino acid sequence, while it is appreciated in the art that nucleotide sequences encode polypeptides. Therefore, one of skill in the art would be subject to undue experimentation to make a Transferrin Receptor Related Apoptosis Inducing Protein (TRRAIP) encoded by SEQ ID NO:1, 2, 3 or 8 to practice the claimed invention.

Similarly, in response to Applicant's argument on pages 29 that test compounds that bind and displace gambogic acid from a Transferrin Receptor Related Apoptosis Inducing Protein (TRRAIP) encoded by SEQ ID NO:1 are

enabled as potentially therapeutic anticancer compounds by this amendment, since one of skill in the art could not make a Transferrin Receptor Related Apoptosis Inducing Protein encoded by SEQ ID NO:1, 2, 3 or 8 to practice the claimed invention, one of skill in the art would be subject to undue experimentation to identify potentially therapeutic anticancer compounds by the claimed methods.

Thus, contrary to Applicant's argument, the amendment to claim 14 has not obviated the ground of rejection set forth in the preceding Office action.

Therefore, for these reasons and as explained more fully in the previous Office action, upon careful and complete consideration of the factors used to determine whether undue experimentation is required, in accordance with the Federal Circuit decision of *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988), the amount of guidance, direction, and exemplification disclosed in the specification, as filed, is not deemed sufficient to have enable the skilled artisan to make and use the claimed invention at the time the application was filed without undue and/or unreasonable experimentation.

New Grounds of Rejection

Claim Rejections - 35 USC § 112

12. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

13. Claims 14, 20-31 and 47 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 14, 20-31 and 47 are indefinite because claim 14 has been amended to recite "a Transferrin Receptor Related Apoptosis Inducing Protein (TRRAIP) *encoded* by SEQ ID NO:1, 2, 3 or 8"; yet SEQ ID Nos:1, 2, 3 and 8 are all amino acid sequences. This renders the claims indefinite because as defined

by Merriam-Webster Online Dictionary, "encode" means, "to specify the genetic code for" (www.m-w.com <http://www.m-w.com>, © 2006-2007 Merriam-Webster, Incorporated viewed 10/2/2007, see Exhibit A) in the biological arts. Merriam-Webster Online Dictionary further defines "genetic code" as "the biochemical basis of heredity consisting of codons in DNA and RNA that determine the specific amino acid sequence in proteins and appear to be uniform for nearly all known forms of life" (www.m-w.com <http://www.m-w.com>, © 2006-2007 Merriam-Webster, Incorporated viewed 10/2/2007, see Exhibit B) Thus as SEQ ID Nos:1, 2, 3 and 8 are not either DNA or RNA sequences it is evident these sequences do not specify the genetic code for a Transferrin Receptor Related Apoptosis Inducing Protein and therefore the metes and bounds of the subject matter that is regarded as the invention cannot be ascertained. Accordingly, due to the nonsensical recitation of a Transferrin Receptor Related Apoptosis Inducing Protein (TRRAIP) *encoded* by an amino acid sequence, it is submitted that the subject matter that is regarded as the invention is unclear to an such an extent that the metes and bounds of the subject matter that is regarded as the invention is not delineated with the clarity and particularity to satisfy the requirement set forth under 35 U.S.C. § 112, second paragraph, so as permit the skilled artisan to know or determine infringing subject matter.

14. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

15. Claims 14, 20-31 and 47 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the

inventor(s), at the time the application was filed, had possession of the claimed invention.

This is a NEW MATTER rejection.

Claim 14 has been amended to recite "a Transferrin Receptor Related Apoptosis Inducing Protein (TRRAIP) *encoded* by SEQ ID NO:1, 2, 3 or 8".

Applicant has indicated that support for the amendment to claim 14 can be found, e.g., in original claim 15 and 19 as filed, paragraphs [0168] to [0227] at pages 88-112 and Example 39 of the specification

Contrary to Applicant's assertion, however, it does not appear that the specification, including the claims, as originally filed, provides written support for the language of the claims.

Though this amendment may be a result of mere oversight, as proteins are encoded by nucleotide sequences and not amino acid sequences, after reviewing the specification, it does not appear that the specification, including the claims, as originally filed, provides adequate support for this amendment.

At paragraph [0055] of the published application, for example, the specification discloses that ""Transferrin Receptor Related Apoptosis Inducing Proteins" and "TRRAIPs" are used interchangeably and refer to SEQ ID NO: 1 or 4". However, this disclosure does not set forth that SEQ ID NO: 1 encodes a TRRAIP given the art-recognized definition of "encode" as set forth above in the rejection of the claims under 35 U.S.C. 112, second paragraph.

Therefore, it is submitted that this clearly illustrates that such amendments have in fact introduced new concepts, thereby violating the written description requirement set forth under 35 U.S.C. §112, first paragraph.

Conclusion

16. No claim is allowed.

17. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

18. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brad Duffy whose telephone number is (571) 272-9935. The examiner can normally be reached on Monday through Friday 7:00 AM to 4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-

free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Respectfully,
Brad Duffy
571-272-9935

/Stephen L. Rawlings/
Stephen L. Rawlings, Ph.D.
Primary Examiner, Art Unit 1643

bd
October 9, 2007

Exhibit A
BD 10/2/07

encode

One entry found.

encode

Main Entry: **en·code**
Pronunciation: \in-'kōd, en-\
Function: *transitive verb*
Date: circa 1919

1 a : to convert (as a body of information) from one system of communication into another; *especially* : to convert (a message) into code **b** : to convey symbolically < capacity of poetry to *encode* ideology — J. D. Niles>
2 : to specify the genetic code for
— **en·cod·er** *noun*

Exhibit B
BD 10/2/07

genetic code

One entry found.

genetic code

Main Entry: **genetic code**
Function: *noun*
Date: 1961

: the biochemical basis of heredity consisting of codons in DNA and RNA that determine the specific amino acid sequence in proteins and appear to be uniform fc nearly all known forms of life